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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/776,936
Filing Date: December 22, 1998
Appellant(s): MILLER ET AL.

Csaba Henter
For Appellant

EXAMINER'S ANSWER

This is in response to the amended appeal brief filed 10/16/06 appealing from the Office action mailed 5/03/05.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

WO 96/25157	Widdowson et al	08-1996

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC 112, First Paragraph

Claims 15-19 are rejected under 35 U.S.C. 1 12, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not give any guidance as to the method of treating cancerous cell growth using the compounds of the instant claims. In re Wands, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 1 12, first paragraph, have been described. They are:

1) Nature of the invention

2) The state of the prior art,

3) The predictability or lack thereof in the ad,

4) The amount of direction or guidance present,

5) The presence or absence of working example,

6) The breadth of the claims,

7) The quantity of the experimentation needed, and

8) The level of the skill in the art.

Nature of the invention: claims 15-19 are directed to method of treating cancerous cell growth mediated by raf kinase, comprising administering the claimed compounds. treatment of tumors and/or cancerous cell growth mediated by raf kinase. In particular, as specified in the instant specification on pages 2-4, the compounds are useful in the treatment of human or animal cancers, e.g., murine, solid cancers, since the progression of these cancers is dependent upon the ras protein signal transduction cascade and therefore susceptible to treatment by interruption of the cascade, i.e., by inhibiting raf kinase. Accordingly, the compounds of the invention are useful in treating solid cancers, such as, for example, carcinomas (e.g., of the lungs, pancreas, thyroid, bladder or colon), myeloid disorders (e.g., myeloid leukemia) or adenomas (e.g., villous colon adenoma). It is understood that the treatment includes humans as well.

The state of the prior art: The state of the prior art is that the pharmacological art involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:
It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific

enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic effects of the above listed diseases, whether or not the disease is effected by the inhibition of raf kinase would make a difference. Appellants' claims include the treatment of any cancer. The state of the prior art is that cancer therapy remains highly unpredictable. The various types of cancers have different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol. It is known that the challenge of cancer treatment has been to target specific therapies to pathogenetically distinct tumor types, that cancer classification has been based primarily on morphological appearance of the tumor and that tumors with similar histopathological appearance can follow significantly different clinical courses and show different responses to therapy. Furthermore, it is known that chemotherapy is most effective against tumors with rapidly dividing cells and that cells of solid tumors divide relatively slowly and chemotherapy is often less effective against them. While the state of the art is relatively high with regard to the treatment of cancerous cell growth, the state of the art with regard to a single agent for treating cancer broadly is underdeveloped. In particular, there is no known anticancer agent, which is effective against cancer such as pancreatic, lung and colon, thyroid or bladder for that matter.

The predictability or lack thereof in the art: The lack of significant guidance from the specification or prior art with regard to the actual treatment of solid cancers in human

subject with the claimed compounds makes practicing the claimed invention unpredictable.

The amount of direction or guidance present: The guidance given by the specification as to how to treat the solid tumor is limited the discussion of the literature only, and various citations have been provided with respect to the corrlationship of in vivo and in vitro inhibition growth with respect to the inhibition of ras kinase. However, the compounds of the claimed subject matter are vastly different than the cited prior art. The guidance provided in the instant specification is as to how to do the assay per the prior art, without substantiating any experimental evidence.

The presence or absence of working examples: All the examples provided in the specification are only drawn to as to how to make the compounds. There is not a single example provided which can point out to the treatment of the solid tumor.

The breadth of the claims: The complex nature of the claims greatly exacerbated by breath of the claims. The claims encompass treating cancerous cell growth mediated by raf kinase broadly.

The quantity of the experimentation needed: Applicants have failed to provide guidance and information to allow the skilled artisan to ascertain which particular type of cancer the claimed anticancer agent is effective against. Applicants have even failed to provide any in vitro data, which can be extrapolated to the in vivo data. Instant claimed compounds are drawn to at least millions of compounds and applicants have not provided as to which will inhibit ras kinase and in turn which compound can be used to treat what type of the cancer.

The level of the skill in the art: The level of ordinary skill in the ad treating the cancerous cell growth is considered to be relatively high. Those responsible for formulating the compositions would be individuals with MS or PhD or MD credentials, or minimally 8-10 years of actual hands on experience.

However, due to the unpredictability in the pharmaceutical art, it is noted that each type of solid tumor or cancer is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which type of cancer would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the instant claims for the treatment of any cell proliferative disorders associated with an altered cell dependent kinase activity. As a result necessitating one of skill to perform an exhaustive search for which diseases can be treated by what compounds of the instant claims in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to

engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

Claims Rejection- 35 USC 103

Claims 1, 3-11, 13, 20-27 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Widdowson et al (WO 9,625,157).

Widdowson et al is teaching structurally similar compounds, composition as claimed herein. See for example page 20, lines 15-20, wherein, X1 can be O or S, R2 can be aryl or hetaryl.

It would have been prima facie obvious to one of ordinary skill in the ad at the time the invention was made to obtain compounds within the generic structure of the reference, because they are structurally so similar to those claimed herein, with the reasonable expectation of achieving a successful pharmaceutical composition, absent evidence to the contrary.

(10) Response to Argument

Appellants' arguments were fully convinced and were not found convincing. Appellants argue that treatment of cancerous cells growth mediated by raf kinase i.e. to treatments that are not objectively doubtable. The examiner disagrees. This may be true for the research purposes only. But this not true for the actual treatment. Had it be true for the actual treatment, cancer would not have been the leading cause of the deaths. Appellants have merely discussed the theoretical aspects of the cancer in the first two pages of the instant specification, without substantiating with respect to their compounds, which are structurally so different to the literature they have cited. It is well

known that many times in vitro studies can hardly be extrapolated to the in vivo studies. Appellants have even failed to provide any in vitro studies, leave alone, the in vivo studies. Appellants allege that Lemoine et al suggests that pancreatic cancer, acute myeloid leukemia, colorectal cancer, thyroid cancer, and non-small-cell lung carcinoma are associated with ras/raf kinase pathway. The examiner does not dispute that indeed Lemoin et al is an overview article, but with respect to the patentability of the instant claimed method, there is no correlationship found in the instant specification.

Appellants allege that on page 74 of the instant specification they have provided data for 144 compounds. What appellants have provided is simply the IC50 data, and examiner would like to point out that there is no explanation that would suggest as to how these data are related to the treatment of various cancers as claimed herein. From the reference cited by the examiner, it can be at most concluded that the instant claimed compounds can be used for treating chemokine mediated diseases, absent evidence to the contrary.

Appellants' arguments were fully considered with respect to 35 USC 103 rejection, and were not found convincing. Appellants admit that a small overlap exists between the substituents defined for L1 herein and the functional groups defined for R in the reference, however, appellants further allege that claims as amended, are distinct from those of Widdowson since the hydroxy substituted group ML1 is not at the ortho position of the phenyl ring. Appellants further allege that there is no motivation to make positional isomer. The examiner disagrees. There is motivation to make positional

isomers, because the positional isomers are prima facie obvious as a whole, absent evidence to the contrary. In re Mehta, 146 USPQ 284. Appellants' arguments that In re Mehta is not a valid citation herein is not convincing. In herein also, there is only substituent which is positionally different, and one of ordinary skill in the art would have made positional isomer, with reasonable expectation of achieving a successful pharmaceutical composition, for treating chemokine mediated diseases, absent evidence to the contrary.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Shailendra Kumar

Conferees:

Sam Barts

Parsa Jafar